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TAUTOMERIC EQUILIBRIA IN SOLUTIONS OF THE PRODUCTS OF REACTION BETWEEN 2-AMINOBENZENESULFONAMIDE AND 3-OXO ALDEHYDES

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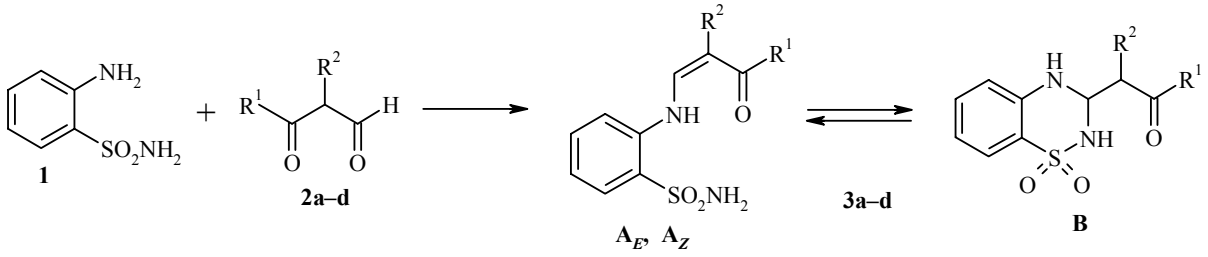
Recently we observed for the first time a ring–chain tautomeric equilibrium for 3-(2-oxoethyl-2-phenyl)-2H,4H-benzothiazine-1,1-dioxides obtained by reaction of 2-aminobenzenesulfonamide with substituted benzoyl acetic aldehydes [1]. With the aim of studying the characteristics of this tautomeric equilibrium in the case of the aliphatic series of keto aldehydes, and also the effect of the substituent at the α-position of the oxo aldehyde, we have studied the reaction of 2-aminobenzenesulfonamide with β-keto aldehydes **2a-d**.

The reaction products obtained, **3a-d,** immediately after dissolving form a tautomeric mixture, represented by the geometric isomers of the enamine form $\mathbf{A}_{E,Z}$. The ratio of *E*- and *Z*-isomers depends significantly on the temperature of the solution. For example, for compound **3a**, $\mathbf{A}_E$:$\mathbf{A}_Z$ = 1:10 at 25°C and 2.5:10 at 80°C. The presence of a substituent at the α-position of the original β-keto aldehyde, as hypothesized in [2], leads to a significant increase in the A_E form, existing in the *s-trans* conformation, which is confirmed by the presence of correlations between the $C\underline{H}_3C$= (1.75 ppm, s) and $COC\underline{H}_2CH_3$ (2.75 ppm, q) signals in the NOESY spectrum of compound **3b**. Over time, a cyclic benzothiazine tautomer **B** appears in the solutions, which for compounds **3b-d** is represented by two diastereomers. The ring–chain equilibrium is established over a period of 4-5 months at room temperature, or within a few days if the solution is held at 80°C. The ratio of the tautomeric forms $\mathbf{A}_E$:$\mathbf{A}_Z$:**B** (the contribution from the diastereomers is given in parentheses) in DMSO solutions having reached equilibrium at 80°C is 2:19:79 for compound **3a**, 56:6:38 (19+19) in the case of **3b**, 34:26:41 (24+17) for **3c**, and 54:22:24 (16+8) for **3d**.



2, 3 a $R^1 = CMe_3$, R^2 = H; **b** R^1 = Et, R^2 = Me; **c** R^1, $R^2 = (CH_2)_4$; **d** R^1, $R^2 = (CH_2)_3$

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2-Aminobenzenesulfonamide was reacted with β-keto aldehydes according to the procedure described earlier in [1]. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 500 (500 MHz and 126 MHz respectively) in DMSO-d6, internal standard TMS. The resonant signals for the benzene ring are not indicated; the R^1 and R^2 signals are indicated only for the major form.

2-(4,4-Dimethylpent-1-enylamino-3-oxo)benzenesulfonamide (3a). Yield 40%; white crystals; mp 143°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): $\mathbf{A}_Z$: 1.12 (9H, s, $(CH_3)_3$); 5.64 (1H, d, $J_{CH–CH}$ = 8.4, C<u>H</u>CO); 7.55-7.60 (1H, m, C<u>H</u>–NH); 7.56 (2H, s, NH_2), 11.93 (1H, d, $J_{NH–CH}$ = 11.8, NH); $\mathbf{A}_E$: 6.29 (1H, d, $J_{CH–CH}$ = 12.7, C<u>H</u>CO); 7.70 (1H, s, NH_2); 7.91 (1H, t, $J_{CH–CH} = J_{CH–NH}$ = 13.0, C<u>H</u>NH); 8.85 (1H, d, $J_{NH–CH}$ = 12.5, NH); **B**: 2.89 (1H, dd, $J_{Ha–CH}$ = 5.0, J_{gem} = 17.5, H-*a* (CH_2)); 3.23 (1H, dd, $J_{Hb–CH}$ = 7.0, J_{gem} = 17.5, H-*b* (CH_2)); 5.12 (1H, m, H-3); 6.97 (1H, s, 4-NH); 7.46 (2H, m, H-8, 2-NH). ^{13}C NMR spectrum, δ, ppm: $\mathbf{A}_Z$: 26.84 (C(<u>C</u>$H_3)_3$), 41.78 (<u>C</u>$(CH_3)_3$); 95.26 (<u>C</u>HCO); 142.25 (CH–NH); 204.85 (CO); $\mathbf{A}_E$: 100.55 (<u>C</u>HCO); 140.79 (CH–NH); 202.32 (CO); **B**: 43.48 (CH_2), 62.20 ($C_{(3)}$), 210.50 (CO). Found: *m*/*z* 282.1036 $[M]^{+\cdot}$. $C_{13}H_{18}N_2O_3S$. Calculated: M = 282.1038.

2-(2-Methylpent-1-enylamino-3-oxo)benzenesulfonamide (3b). Yield 40%; yellowish crystals; mp 209°C. ^{1}NMR spectrum, δ, ppm (*J*, Hz): $\mathbf{A}_E$: 1.02 (3H, t, $J_{CH_2–CH_3}$ = 7.2, CH_3); 1.75 (3H, s, CH_3C=C); 2.75 (2H, q, $J_{CH_2–CH_3}$ = 7.2, CH_2); 7.73 (2H, s, NH_2); 8.05 (1H, d, $J_{CH–NH}$ = 11.6, C<u>H</u>–NH); 8.76 (1H, d, $J_{NH–CH}$ = 12.0, NH); $\mathbf{A}_Z$: 1.97 (3H, s, CH_3C=C); 7.35 (1H, d, $J_{CH–NH}$ = 11.6, <u>C</u>H–NH); 7.45 (2H, s, NH_2); 11.80 (1H, d, $J_{NH–CH}$ = 11.6, N<u>H</u>–CH); **B**: 2.99-3.05 (1H, s, CH_3C<u>H</u>); 4.80 and 5.00 (1H, dd, $J_{CH–CH}$ = 8.1, $J_{CH–NH}$ = 12.0, H-3); 6.90 and 6.92 (1H, s, 4-NH); 7.44 and 7.48 (1H, d, $J_{NH–CH}$ = 12.0, 2-NH). ^{13}C NMR spectrum, δ, ppm: $\mathbf{A}_E$: 8.87 (<u>C</u>H_3C=C); 9.42 (<u>C</u>H_3CH_2); 28.92 (CH_2); 112.73 (=<u>C</u>–CO); 136.91 (CH–NH); 198.22 (CO); $\mathbf{A}_Z$: 102.12 (=<u>C</u>–CO); 138.69 (CH–NH); 201.14 (CO); **B**: 48.39 and 48.66 (CH_3<u>C</u>H), 66.15 and 67.08 (C-3), 210.34 and 210.90 (CO). Found, *m*/*z* 268.0877 $[M]^{+\cdot}$. $C_{12}H_{16}N_2O_3S$. Calculated: M = 268.0882.

2-((2-Oxocyclohexylidenyl)methylamino)benzenesulfonamide (3c). Yield 51%; yellow crystals; mp 181°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): $\mathbf{A}_E$: 1.70-1.80 (4H, m, 2H-4', 2H-5'); 2.24-2.32 (2H, m, 2H-3'); 2.35-2.45 (2H, m, 2H-6'); 7.73 (2H, s, NH_2); 7.92 (1H, dm, $J_{CH–NH}$ = 13.2, CH); 8.78 (1H, d, $J_{NH–CH}$ = 12.8, NH); $\mathbf{A}_Z$: 7.36 (1H, dm, $J_{CH–NH}$ = 11.6, C<u>H</u>–NH); 7.45 (2H, s, NH_2); 11.99 (1H, d, $J_{NH–CH}$ = 11.6, N<u>H</u>–CH); $\mathbf{B_1}$: 4.94 (1H, dd, $J_{CH–NH}$ = 12.0, $J_{CH–CH}$ = 8.0, H-3); 6.78-6.82 (2H, m, H-5, NH-4); 7.38 (1H, d, $J_{NH–CH}$ = 12.0, NH-2); $\mathbf{B_2}$: 5.20 (1H, dd, $J_{CH–NH}$ = 12.5, $J_{CH–CH}$ = 3.0, H-3); 6.90 (1H, s, 4-NH); 7.43 (1H, d, $J_{CH–NH}$ = 13.0, 2-NH). ^{13}C NMR spectrum, δ, ppm: $\mathbf{A}_E$: 22.09 ($C_{(4')}$); 22.34 ($C_{(5')}$); 23.36 ($C_{(6')}$); 38.62 ($C_{(3')}$); 111.76 ($C_{(1')}$); 133.91 (CH–NH); 137.88 ($C_{(2)}$); 196.32 (CO); $\mathbf{A}_Z$: 108.03 ($C_{(1')}$); 139.52 (<u>C</u>H–NH); 198.67 (CO); $\mathbf{B_1}$: 64.18 ($C_{(3)}$); 209.41 (CO); $\mathbf{B_2}$: 63.56 ($C_{(3)}$); 208.51 (CO). Found: *m*/*z* 280.0884 $[M]^{+\cdot}$. $C_{13}H_{16}N_2O_3S$. Calculated: M = 280.0882.

2-((2-Oxocyclopentylidenyl)methylamino)benzenesulfonamide (3d). Yield 45%; light yellow crystals; mp 175°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): $\mathbf{A}_E$: 1.90-1.96 (2H, m, 2H-4'); 2.22-2.28 (2H, m, 2H-3'); 2.56 (2H, m, 2H-5'); 7.72 (1H, m, CH); 7.74 (2H, s, NH_2); 8.70 (1H, d, $J_{NH–CH}$ = 13.2, N<u>H</u>); $\mathbf{A}_Z$: 7.44 (1H, dm, $J_{CH–NH}$ = 11.4, C<u>H</u>–NH); 7.49 (2H, s, NH_2); 11.23 (1H, d, $J_{NH–CH}$ = 12.0, N<u>H</u>–CH); $\mathbf{B_1}$: 4.98 (1H, dd, $J_{CH–NH}$ = 12.0, $J_{CH–CH}$ = 5.4, H-3); 7.02 (1H, s, 4-NH); 7.34 (1H, d, $J_{NH–CH}$ = 12.0, 2-NH); $\mathbf{B_2}$: 5.10 (1H, dd, $J_{CH–NH}$ = 12.3, $J_{CH–CH}$ = 2.7, H-3); 6.82 (1H, s, 4-NH); 7.58 (1H, d, $J_{CH–NH}$ = 12.6, 2-NH). ^{13}C NMR spectrum, δ, ppm: $\mathbf{A}_E$: 19.32 ($C_{(4')}$); 24.91 ($C_{(5')}$); 38.35 ($C_{(3')}$); 113.71 ($C_{(1')}$); 129.97 (CH–NH); 204.12 (CO); $\mathbf{A}_Z$: 134.34 (CH–NH); 205.36 (CO); $\mathbf{B_1}$: 65.17 ($C_{(3)}$); 216.40 (CO); $\mathbf{B_2}$: 63.83 ($C_{(3)}$); 215.79 (CO). Found: *m*/*z* 266.0718 $[M]^{+\cdot}$. $C_{12}H_{14}N_2O_3S$. Calculated: M = 266.0725.

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